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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/718,833	11/21/2003	Charles Wilson	23239-541 (ARC-41)	3645

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EXAMINER	
ASHEN, JON BENJAMIN	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 08/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/718,833	WILSON ET AL.	
	Examiner	Art Unit	
	Jon B. Ashen	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-57 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-57 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-10, drawn to a high molecular weight aptamer composition comprising a nucleic acid comprising two or more aptamers and a stabilizing moiety that comprises a linking moiety that is not a nucleic acid molecule, classifiable in class 536, subclass 23.1.

II. Claims 11-15, drawn to a high molecular weight aptamer composition comprising a nucleic acid moiety comprising two or more aptamer domains joined by a linker domain and a stabilizing moiety comprising one or more attached polyalkylene glycol moieties attached to the linker domain, classifiable in class 536, subclass 23.1.

III. Claims 16-35, drawn to a high molecular weight aptamer composition comprising a nucleic acid comprising two or more aptamer domains joined by a linker domain and a stabilizing moiety comprising an oligonucleotide splint which hybridizes to at least a portion of the linker domain, classifiable in class 536, subclass 23.1.

IV. Claims 36-40 and 53-57, drawn to therapeutic high molecular weight aptamer compositions comprising the aptamer compositions of claims 1, 11, 16, 21 or 28 and methods of treating a disease in a subject by administering therapeutic high molecular weight aptamer compositions comprising the aptamer compositions of claims 1, 11, 16, 21 or 28, classifiable in 514, subclass 44.

V. Claims 41-44, drawn to a high molecular weight aptamer composition comprising an aptamer and two or more non-nucleic acid stabilizing moieties, classifiable in class 536, subclass 23.1.

VI. Claims 46-52, drawn to a method of improving the pharmacokinetic properties of an aptamer therapeutic composition comprising introducing reactive groups in a nucleic acid aptamer, reacting said groups with reactive groups on a stabilizing moiety, thereby forming a stabilized aptamer, classified in class 536, subclass 25.3.

2. The inventions are distinct, each from the other because of the following reasons:

3. Inventions I-III and V are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). Invention I is drawn to a high molecular weight aptamer composition comprising a

nucleic acid comprising two or more aptamers and a stabilizing moiety that comprises a linking moiety that is not a nucleic acid molecule. Invention II is drawn to a high molecular weight aptamer composition comprising a nucleic acid moiety comprising two or more aptamer domains joined by a linker domain and a stabilizing moiety comprising one or more attached polyalkylene glycol moieties attached to the linker domain. Invention III is drawn to a high molecular weight aptamer composition comprising a nucleic acid comprising two or more aptamer domains joined by a linker domain and a stabilizing moiety comprising an oligonucleotide splint which hybridizes to at least a portion of the linker domain. Invention V is drawn to a high molecular weight aptamer composition comprising an aptamer and two or more non-nucleic acid stabilizing moieties. In the instant case the different inventions are not disclosed as capable of use together and have different functions based on the different chemical structures of the components comprised by each invention. Invention I functions to stabilize two or more aptamers in a composition using a linking moiety that is not a nucleic acid molecule. Invention II functions to stabilize a two or more aptamer domains that are joined by a linker domain using a stabilizing moiety that comprises polyalkylene glycol attached to the linker domain. Invention III functions to stabilize a nucleic acid comprising two or more aptamer domains and a linker domain using an oligonucleotide splint that hybridizes to the linker domain. Invention V functions to stabilize a single aptamer using two or more non-nucleic acid stabilizing moieties. "Linker domain" is interpreted as reading on nucleic acid domains because it is not set forth by limiting definition and is used, in the context of the specification, as a nucleic acid domain that links two aptamer

domains and that is hybridized by the claimed oligonucleotide splint. Linker domain is distinguished from linking moiety because the linking moiety is specifically set forth in claim 1 as being "not a nucleic acid molecule."

Furthermore, searching any of inventions I-III or V together would impose a serious and undue administrative burden. In the instant case, prior art searches of each composition are not coextensive. Search of each of these inventions would require different key word searches for particular components comprised by each composition that were not comprised by the other compositions, using divergent patent and non-patent literature databases. A search, for example, of Invention I would require a search of non-nucleic acid linking moieties that would not be required by a search of inventions II or III. Each search would then require subsequent in-depth analysis of all relevant prior art literature, placing an undue and serious burden on the Office in terms of both search and examination. As such, it would be burdensome to perform search and examination of any of Inventions I-III or V together.

4. Inventions I-III and VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). Inventions I-III are relied upon as above. Invention VI is drawn to a method of making a stabilized aptamer. In the instant case the different inventions are not disclosed as capable of use together and have different functions. Invention I functions to stabilize two or more aptamers in a composition using a linking moiety that is not a nucleic acid

molecule. Invention II functions to stabilize a two or more aptamer domains that are joined by a linker domain using a stabilizing moiety that comprises polyalkylene glycol attached to the linker domain. Invention III functions to stabilize a nucleic acid comprising two or more aptamer domains and a linker domain using an oligonucleotide splint that hybridizes to the linker domain. Invention VI functions to provide a method of making a stabilized aptamer by specified protocol comprising introducing reactive groups to aptamers.

Furthermore, searching any of inventions I-III or VI together would impose a serious and undue administrative burden. In the instant case, prior art searches of each composition and a method of making a stabilized aptamer would not be coextensive. Search of each of these inventions would require different key word searches for particular components comprised by each composition that and for the distinctive steps required to make the stabilized aptamer that were not required for the other Inventions, using divergent patent and non-patent literature databases. Each search would then require subsequent in-depth analysis of all relevant prior art literature, placing an undue and serious burden on the Office in terms of both search and examination. As such, it would be burdensome to perform search and examination of any of Inventions I-III or VI together.

5. Inventions I-III and group IV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially

different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). Inventions I-III are relied upon as above. Group IV is drawn to three patentably distinct therapeutic high molecular weight aptamer compositions (as will be set forth below) comprising the aptamer compositions of claims 1, 11, 16, 21 or 28 and methods of treating a disease in a subject by administering such. In the instant case, each of the products as claimed can be used in a materially different process of using those products, which would be an in vitro assay to determine the levels of PDGF or TGF-ß2 protein expression.

Furthermore, searching any of Inventions I-III with any of the inventions of Group IV together would impose a serious and undue search burden. In the instant case, a prior art search of methods of treatment using aptamer compositions would not be coextensive with a prior art search of the claimed aptamer compositions. Search of each of these inventions would require different key word searches of the compositions and methods of using said compositions and would require, at least, a search for distinctive steps necessary to practice the instantly claimed methods or to administer the instantly claimed therapeutic compositions, in divergent patent and non-patent literature databases, that would not be required in a search of the claimed high molecular weight aptamer compositions that are not claimed as therapeutic. The different searches would then require subsequent in-depth analysis of the relevant prior art literature, placing an undue and serious administrative burden on the Office in terms of both search and examination. As such, it would be burdensome to perform examination any of Inventions I-III together with any of the inventions in Group IV.

6. Inventions IV and V are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are unrelated because the aptamer composition that is Invention IV is shown to be unrelated to the aptamer compositions of inventions I-III (as set forth in section 4 above) and Invention V is drawn to the process of use of the aptamer compositions that are Inventions I-III.

Furthermore, searching Inventions IV and V together would impose a serious and undue search burden. In the instant case, neither a prior art search of methods of treatment using aptamer compositions nor the prior art searches for the structures required in the aptamer compositions of inventions I-III, that are required to formulate the therapeutic compositions and to practice the methods encompassed in Invention V, would not be coextensive with a prior art search of the aptamer composition of Invention IV. Search of each of these inventions would require different key word searches of the structures required by the compositions and methods of using said compositions and would require, at least, a search for distinctive steps necessary to practice the instantly claimed methods or to administer the instantly claimed therapeutic compositions, in divergent patent and non-patent literature databases, that would not be required in a search of the claimed high molecular weight aptamer compositions that are not claimed as therapeutic. The different searches would then require subsequent in-depth analysis of the relevant prior art literature, placing an undue and serious administrative burden

on the Office in terms of both search and examination. As such, it would be burdensome to perform examination of Inventions IV and V together.

7. Inventions V and VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). Inventions V and Vi are relied upon as above. In the instant case, the Inventions are not disclosed as capable of use together have different functions. Invention V functions as a composition of aptamers that are stabilized by two or more non-nucleic acid moieties. Invention VI functions to provide a method of making a stabilized aptamer by specified protocol comprising introducing reactive groups to aptamers.

Furthermore, searching Inventions V and VI together would impose a serious and undue search burden. In the instant case, a prior art search of aptamer compositions comprising non-nucleic acid stabilizing moieties and a prior art search for specified method steps required to practice a method of making a stabilized aptamer would not be coextensive. Search of each of these inventions would require different key word searches of the structures required by the composition and the distinctive steps necessary to practice the instantly claimed method, in divergent patent and non-patent literature databases. The different searches would then require subsequent in-depth analysis of the relevant prior art literature, placing an undue and serious administrative burden on the Office in terms of both search and examination. As such, it would be burdensome to perform examination of Inventions IV and VI together.

8. Inventions IV and VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). Inventions IV and VI are relied upon as above. In the instant case, the Inventions are not disclosed as capable of use together have different functions. Invention IV functions as therapeutic compositions and methods of treatment using the aptamer compositions of Inventions I-III. Invention VI functions to provide a method of making a stabilized aptamer by specified protocol comprising introducing reactive groups to aptamers.

Furthermore, searching Inventions IV and VI together would impose a serious and undue search burden. In the instant case, a prior art search of therapeutic compositions and methods of treatment using the aptamer compositions of Inventions I-III and a prior art search for specified method steps required to practice a method of making a stabilized aptamer would not be coextensive. Search of each of these inventions would require different key word searches of the structures required by the therapeutic compositions and the distinctive steps necessary to practice the instantly claimed methods of treatment that would not be required for the distinctive steps necessary to practice a method of making a stabilized aptamer, in divergent patent and non-patent literature databases. The different searches would then require subsequent in-depth analysis of the relevant prior art literature, placing an undue and serious administrative burden on the Office in terms of both search and examination. As such, it would be burdensome to perform examination of Inventions IV and VI together.

9. Groups I-III are further restricted as follows:

10. Claims 7-8, 13-14, 18-19, 25-26 and 33-34 specifically claim patentably distinct high molecular weight aptamer compositions that comprise aptamers which are targeted to and which bind specified proteins (either PDGF or TGF-ß2). However, the aptamer sequences claimed each target and bind different proteins and are considered to be unrelated since each aptamer sequence claimed is structurally and functionally independent and distinct for the following reasons: each aptamer sequence has a unique nucleotide sequence, each aptamer sequence targets a different protein and a different and specific region of that protein, either PDGF or TGF-ß2 and binds thereto. Each aptamer, upon binding to its respective protein target (PDGF or TGF-ß2), will functionally modulate the activity of that different protein, absent evidence to the contrary. If electing one of Inventions I-III, Applicant is requested to elect a single target protein of the claimed aptamer composition, either PDGF or TGF-ß2, which will be examined in its full scope including all claims readable thereon.

11. Group IV is further restricted as follows:

12. Claims 36-40 and 53-57 specifically claim patentably distinct therapeutic compositions and methods of treatment comprising the patentably distinct high molecular weight aptamer compositions of a) Invention I, claim 1; b) Invention II, claim 11 and c) Invention III, claims 16, 21 and 28 (as set forth above). Upon election of group IV, Applicant is requested to elect a single patentably distinct therapeutic

composition and method of treatment which will be examined in its full scope including all claims readable thereon.

13. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996).

Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon B. Ashen whose telephone number is 571-272-2913. The examiner can normally be reached on 7:30 am - 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's acting supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Jba

Jane Zara
TC 1600